REMARKS

Claims 21, 31 and 32 have been amended and new claims 33-42 have been added. No additional claims fees are required. In consideration of the claim amendments and the arguments presented herewith, reconsideration of the application is respectfully requested.

Claims 21-23 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Each of these rejections has been addressed in the amendments presented herewith. With these rejections being obviated, reconsideration thereof is respectfully requested.

The Examiner has further rejected Claims 21-24, 28, 30 and 32 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,704,354 to Preidel, et al. (henceforth referred to as Preidel). The Examiner alleges that Preidel teaches an implantable glucose sensor in a host where the implantation is for a period of over 360 days. With respect to claim 32, the Examiner alleges that the Preidel sensor would be in contact with a foreign body capsule.

Applicants respectfully traverse the rejection under §102(e) on the grounds that (1) Preidel fails to teach or suggest, *inter alia*, a wholly implantable device as provided by the present invention, (2) Preidel fails to teach or provide an enabling description of "continuous glucose sensing", and (3) the Preidel device as disclosed would not be capable of continuous glucose sensing in either blood vessels or subcutaneously as defined in the present invention. These points will now be addressed in further detail below.

The electrocatalytic sensor of Preidel is of a catheter type of construction for determining glucose in body fluids, especially in the blood. Catheters are well-known in the medical arts for use in drawing body fluids from a patient. In column 1, lines 65-67 of Preidel, the device includes as one of its components "lead wires to the electrodes arranged within the

tubular body which are brought to the outside through the other end of the tubular body." As noted by the Examiner, "Preidel does not use telemetry to transmit the signal out of the body." In fact, it is well-known in the art that a catheter type sensor such as the Preidel sensor would be electrically connected to a glucose monitor located outside the patient's body by means of the lead wires of the device. Thus, in contrast to the present invention, as, for example, recited in claim 31, the Preidel device is not wholly implantable in that the patient needs to remain electrically connected to a monitor in order to continue to receive information from the device. Because of the well-known risk of serious infection, such a device is primarily useful for bedside monitoring of the patient.

Moreover, Preidel fails to teach or provide an enabling disclosure of "continuous glucose sensing". In particular, Column 1, lines 19 and 20 of Preidel merely indicate a need in the art for long-term stability. Column 1, lines 44 and 45 of Preidel simply states that the sensor "has the long-term stability necessary for an implant". Taken together, these passages do not provide sufficient enabling disclosure to demonstrate long-term stability of over 30 days as defined by Applicants' specification, and as now claimed by Applicant in claim 21.

In particular, on page 9, lines 20-25 of Applicants' specification, it states: "The phrase 'continuous glucose sensing' refers to the period in which monitoring of plasma glucose concentration is continuously carried out. More specifically, at the beginning of the period in which continuous glucose sensing is effected, the background sensor output noise disappears, and the sensor output stabilizes (e.g., over several days) to a long-term level reflecting adequate microcirculatory delivery of glucose and oxygen to the tip of the sensor." Furthermore, on page 10, lines 1-2 of Applicants' specification, it states "Failure of adequate vascularization or consistent contact of tissue with sensor will result in failure of continuous glucose sensing." Claims 21, 28, 30, 31, 32 and 38 all, for example, call for a method wherein the device is capable of continuous glucose sensing, none of which are or can be anticipated by Preidel.

The present invention describes an implantable device suitable for long-term continuous glucose sensing as defined in Applicants' specification. In particular, the present inventors have recognized that Foreign Body Capsule (FBC) formation is the dominant event surrounding long-term implantation of any sensor and that the formation must be enhanced to support sensor performance. The unique architecture of the device of the present invention allows for there to be a dependable flow of blood to deliver glucose to the implanted device at a concentration representative of that in the vasculature. This is accomplished *via* a layer that serves to promote vascularization in the sensor interface region as now set forth in claim 38.

Moreover, the devices of the present invention become secured with the tissue of the subject by means of a capsular attachment layer, thereby reducing or eliminating "motion artifact", which contributes to unreliable results. This is accomplished by using materials, such as surgical-grade polyester velour, that encourage Foreign Body Capsule tissue to aggressively grow into the materials and form a strong mechanical bond. This fixation of the implant in its capsule is essential to prevent "motion artifact" which contributes to unreliable results. The non-smooth surface of the capsular attachment layer 16 is shown in Figure 1B of Applicants' specification.

In contrast to the present invention, the Preidel device is a smooth surface device that, if implanted subcutaneously, would evoke a classical foreign body capsule, such that long-term availability of glucose to the sensor would be blocked. In particular, the tubular body of the device in contact with the tissue is disclosed as being preferably silicone, which as commonly known in the art would be smooth in texture. The Preidel device neither discloses nor suggests the use of an angiogenic layer or equivalent to promote the microcirculatory delivery of glucose and oxygen to the sensor tip, which is necessary for continuous glucose sensing as defined in Applicants' specification. Furthermore, the Preidel device does not include a capsular attachment layer or any other securing means, and as such would be

susceptible to "motion artifact", which as described above and in Applicants' specification would contribute to unreliable results. Thus, this device would not be useful for continuous long-term monitoring of glucose.

In this regard, with specific reference to the rejection of claim 32, Applicant notes that amended claim 32 now recites that the sensor tip is substantially fixated in its foreign body capsule. This amendment does not constitute new matter. As described above, the Preidel device teaches a smooth surface implant that would evoke a classical foreign body capsule. However, due to the lack of any equivalent of an angiogenic layer or capsular attachment layer, the sensor tip of the Preidel device would not be substantially fixated in its foreign body capsule, as would be the case for the present invention.

In addition, practical size limitations exist that directly effect wholly implanted sensor performance. The Preidel device requires a sensing region of 90 mm^2. Preidel specifies dimensions of between 30 to 80 cm for the sensor and catheter alone, with the sensor occupying about 5 cm of length. These overall dimensions would not be suitable for subcutaneous implantation. In contrast, the entire housing of the device of the present invention (which includes a circuit board and electrodes) is approximately 1.4 cm x 7.0 cm. Thus, a device of the present invention would be suitable for subcutaneous implantation.

Moreover, with regard to the suitability of the Preidel device for continuous glucose monitoring in blood, as noted in Applicants' specification at page 2, lines 6-8, probes that are placed directly into the vasculature put the recipient at risk for thrombophlebosis, thromboembolism, and thrombophlebitis. Moreover, it is well-known in the art that the lumens of long-term indwelling catheters like Preidel's are subject to occlusions that appear to consist of fibrin-based clots or lipid-based substances. When an occlusion or any of these other complications occur, the catheter must be replaced or the lumen must be cleared in order to resume normal function of the device. It is further well-known in the art that catheter-like

pacemaker leads which reside in veins in a way consistent with Preidel are covered after months of implantation with a foreign body like sheath that would hamper dependable flow of analyte to the sensing region. Thus, the Preidel sensor would not seem to be suitable for long-term continuous glucose monitoring, as has been defined by Applicants.

The Examiner has further rejected claim 29 under 35 U.S.C. §103(a) as being unpatentable over Preidel, et al. Applicants respectfully traverse this rejection on the grounds that there is no teaching or suggestion in Preidel regarding calibration.

The Examiner has also rejected claim 31 under 35 U.S.C. §103(a) as being unpatentable over Preidel et al in view of Ward et al. Applicants respectfully traverse this rejection on the grounds that there is no suggestion in either the Preidel or Ward reference to combine the teachings therein.

Having responded in full to the present Office Action, it is respectfully submitted that the application is in condition for allowance. Favorable action thereon is respectfully solicited.

Pursuant to §1.56, attached hereto is form PTO-1449 identifying additional references which have come to the attention of the undersigned. Since these references are being submitted after receipt of a first Office Action under §1.97(c), please charge the required fee of $180.00 to our Deposit Account No. 08-2461.

Should the Examiner have any questions, the Examiner is invited to call the undersigned at the telephone number listed below.

Respectfully submitted,

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VERSION OF AMENDMENT WITH MARKINGS SHOWING CHANGES

IN THE CLAIMS:

Please amend the claims as follows:

21. (Amended) A method of monitoring glucose levels, comprising:

a) providing i) a host, and ii) a device comprising a housing and means for determining the amount of glucose in a biological fluid; and

b) implanting said device in said host under conditions such that said device measures said glucose accurately for a period of time exceeding about 30 days to exceeding about 360 days.

31. (Amended) A method of measuring glucose in a biological fluid, comprising the steps of: providing i) a host, and ii) an implantable device comprising a sensor capable of continuous glucose sensing; implanting said device wholly subcutaneously in said host and transmitting data by telemetry from said wholly implantable device to an external device.

32. (Amended) A method of measuring glucose in a biological fluid, comprising the steps of:

a) providing a host:

b) providing an implantable device comprising a sensor capable of continuous glucose sensing, said sensor having an interface tip;

c) implanting said device subcutaneously into tissue of said host so as to elicit a foreign body capsule as a result of the response of said host to the introduction of said implantable device, said sensor interface tip communicating with the tissue of said host such that said tip is [in intimate contact with] substantially fixated in said foreign body capsule.

Please add the following new claims 33-42:

33. (New) A method according to claim 32, wherein said device is wholly implanted subcutaneously in said host.

34. (New) A method according to claim 32, wherein said sensor tip is substantially fixated in said foreign body capsule by the provision of a capsular attachment layer on said sensor.

35. (New) A method according to claim 34, wherein said sensor tip is further substantially fixated by the provision of an angiogenic layer on said sensor.

36. (New) A method according to claim 34, wherein said capsular attachment layer is non-smooth.

37. (New) A method according to claim 36, wherein said non-smooth layer includes surgical grade polyester velour.

38. (New) A method of monitoring glucose levels, comprising:

a) providing i) a host, and ii) a device comprising a housing and a sensor capable of continuous glucose sensing, said sensor including a vascularization promotion layer; and

b) wholly implanting said device subcutaneously in said host under conditions such that said device provides continuous glucose sensing.

39. (New) A method according to claim 38, wherein said vascularization promotion layer is an angiogenic layer.

40. (New) A method according to claim 38, wherein said sensor further includes a capsular attachment layer.

41. (New) A method according to claim 38, wherein said implant is sized and configured for being wholly implanted subcutaneously.

42. (New) A method according to claim 41, further including the step of transmitting data from said wholly implanted device telemetrically.